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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	15

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/485,245	Hopkins, A
Examiner	**Art Unit**
CB Wilder	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Jul 20, 2001*.

2a) X This action is **FINAL.** 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-6* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) X Claim(s) *1-6* is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are objected to by the Examiner.

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) X Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) X All b) Some* c) None of:

1. X Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15	Notice of References Cited (PTO-892)	18	Interview Summary (PTO-413) Paper No(s).
16	Notice of Draftsperson's Patent Drawing Review (PTO-948)	19	Notice of Informal Patent Application (PTO-152)
17	Information Disclosure Statement(s) (PTO-1449) Paper No(s).	20	Other

FINAL ACTION

1. Applicant's request for reconsideration filed July 20, 2001 in Paper No. 13 is acknowledged. Claims 1-6 are pending. The arguments have been thoroughly reviewed but they are not found persuasive for the reasons that follows. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims.

This Action is made FINAL.

2. The text of those sections of title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejections under 35 U.S.C. 103(a) directed to claims 1-5 as being unpatentable over Suganuma et al. in view of Shen et al. is maintained and discussed below. The prior art rejection under 35 U.S.C. 103(a) directed to claim 6 as being unpatentable over Suganuma et al. in view of Shen et al. and further in view of Hoeltke et al. and further in view of Strategene is maintained and discussed below.

Claim Rejections - 35 USC § 103

4. Claims 1- 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suganuma et al. (Analytical Biochemistry January 20, 1995), and further in view of Shen et al (EP 0 726 310 August 14, 1996). Regarding claims 1, 2 and 4, Suganuma et al. also teach a labeling composition

comprising a random mixture of oligonucleotides which are 5 mers to 11 mers (page 605, col. 2, lines 36 and 37). Suganuma et al. teach wherein the composition further comprise a polymerase enzyme, a supply of nucleotides for chain extension, a labeled nucleotide and buffer (page 606, lines 1-10). The composition Suganuma et al. differ from that of the claimed invention in that the references do not teach wherein a dye and/or stabilizer is added to the composition. In a composition similar to that of Suganuma et al., Shen et al. teach wherein the composition is present in a dry state. Shen et al. also teach wherein the composition comprise a stabilizer along with a polymerase enzyme and a supply of nucleotides for chain extension (page 6, lines 3-7 and 22). Shen et al. do not expressly teach the incorporation of a dye. However, the use of dyes as labeling agents was routinely practiced in the art. It would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to add a stabilizer to the labeling composition of Suganuma et al.. One of ordinary skill in the art would have been motivated to do for the expected benefits taught by Shen et al. that a stabilizing agent prevents or delays the loss of a composition's biological activity as a result of storage over time (page 4, lines 8-10). One of ordinary skill in the art would have been motivated further to add a dye for labeling in view of routine art practice for the obvious benefit of visualizing a polynucleotide generated with the composition.

Regarding claim 3, Suganuma et al. teach, wherein the random mixture is of 6 mer oligonucleotides (page 605, col. 2, lines 36 and 37).

Regarding claim 5, Suganuma et al. in view of Chen et al. teach a method of making a labeled probe for a nucleic acid template, wherein the method comprises the steps of providing a

nucleic acid template and labeling composition and incubating the nucleic acid template under chain extension conditions with the labeling composition (bottom of page 605, beginning at line 38 to page 606, lines 1 1-11).

5. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Suganuma et al. in view of Shen et al. in view of Hoeltke et al. (5,814,502, effective filing date October 1994) and further in view of Strategene (January 1997). Regarding claim 6, Suganuma et al. in view of Shen et al. teach a labeling composition and method of making a labeled probe comprising a number of method steps wherein the labeled compositions comprises a random mixture of oligonucleotides which are 6 mers to 8-mers, and said composition present in a dry state. The labeling composition of the disclosure differs from that of the references in that the references do not expressly teach the concentration of the random mixture of oligonucleotides. However the optimal contents range would have been determined by the practitioner based on desired properties of the random oligonucleotides, desired lengths of the random oligonucleotides and desired results. For example, in a method for labeling nucleic acid, Hoeltke et al. teach a random mixture of oligonucleotides wherein the concentration range of approximately 15 to 80 OD/ml is selected for the various random primers which are 6-mers to 15- mers. Hoeltke et al. further teach that depending on the primer length, the optimal contents range will change (col. 2, lines 55-60 and col. 3, lines 38-42). Strategene teaches a labeling composition comprising mixture of oligonucleotides which are 7-mers to 8-mers wherein the mixture of oligonucleotides are present at a concentration of about 1 OD/ml to 10 OD/ml. In view of the foregoing, it would have been obvious to one of ordinary skill in the

art that the concentration range of the random mixture of oligonucleotide may vary based the practitioner's preference as well as the length of the primers as suggested by Hoeltke et al.

6. Applicant traverses the rejection on the following grounds: Applicant argues that the claimed invention is directed to dried mixtures of random primers and relates to the discovery that sel annealing occurs when random 9-mers and (longer oligonucleotides) are used in dried predispersed labeling kit. Applicant argues that this problem is specific to dried 9-mers and longer oligonucleotides and does not represent a problem with shorter dried primers. Applicant states that evidence showing this effect with dried primers is presented as reflected in self priming activity and labeling intensity in the examples within the specification as discussed in the interview. Applicant argues that while the prior art discloses primers of various length including dried primer preparation, there is no disclosure by Suganuma of dried compositions or teaching that self annealing represented a limitation for dried primer composition. Applicant continues by stating that moreover, the art failed to teach that dried 6-mer to 8-mer compositions would be preferred to longer dried primers because of the general prejudice in the art that longer primers were preferable to shorter primers because longer primers have higher hybridization melting temperatures and are more stable and specific. Applicant argues that while Suganuma identified the occurance of self annealing in longer primers in solution, there was no suggestion by Suganuma or expectation in the art that self annealing occurs when random 9-mers are used in dried predispersed labeling kits and this limits their stability and shelf life. Finally, Applicant argues the Shen et al., Hoeltke et al. or Stratagene references do not teach 6-mer to 8-mer compositions as claimed in the instant invention. Applicant

argues that the secondary references fail to make up the deficiency in Suganuma and the rejections under 103(a) should be withdrawn.

7. The arguments have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follows: Firstly, In response to Applicant's argument that the references fail to show teaching that self-annealing represents a limitation for dried primer compositions, it is noted that the features upon which Applicant relies (i.e. limitation of self-annealing) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, the argument that there is a general prejudice in the art that longer primers are preferable to shorter primers because longer primers have higher hybridization melting temperature and are more stable and specific is irrelevant to the instant invention because the reference of Suganuma et al. teach random primers of comparable size as those claimed in the instant invention. The court have established in *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955) that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation". The court has established that "a claim which falls within the broad scope of the references is held unpatentable thereover because, among other reasons, there is no evidence of the **criticality** of the claimed ranges" (See *in re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA)). Therefore, as noted in the prior Office Action, the random mixture of oligonucleotides (6-mer to 8-mer) of the claimed invention falls *within* the range of the random mixture of oligonucleotides (5-mer to 11-mer)

of Suganuma. The reference does not teach the composition in a dry state, however dry compositions are well known in the prior art as taught by Shen et al. Shen et al. teach methods of preparing composition comprising oligonucleotides in dried state (page 15, Example 6). Shen et al. also teach wherein the composition comprise a stabilizer along with a polymerase enzyme and a supply of nucleotides for chain extension (page 6, lines 3-7 and 22). The references of Hoeltke et al. and Strategene are provides limitations not found in the primary reference of Suganuma et al. The arguments are not sufficient to overcome the prior art rejection. Accordingly, the rejections under 35 U.S.C. 103(a) are maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The Examiner can normally be reached on Monday through Thursday from 7:00 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Exr.'s supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder

Cynthia B. Wilder, Ph.D.

September 18, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

9/20/01